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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FIELD, TAMMY K	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,068	ALPAR ET AL.	
	Examiner	Art Unit	
	Tammy K. Field	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 26* is/are pending in the application.

4a) Of the above claim(s) *14-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amended claims (1-13) and new Claim 26 received in the Office March 22, 2004 are presently under consideration.

2. Group I (Claims 1-13) and species election of Claim 1(ii)(C), positively charged cationic pluronics ® is now amended to read on "a positively charged cationic block copolymer or a positively charged cationic surfactant".

3. Newly submitted claim 26 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the complexing agent; or the clathrate read on non-elected species E) and D) of Group I.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 26 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Priority

5. The priority date is set at March 24, 1999.

Information Disclosure Statement

6. The supplemental information disclosure statement filed on March 22, 2004 has been considered. An initialed copy is enclosed.

Status of Claim Objections

7. Claims objections due to informalities are withdrawn:

a. Claims 3 and 11.

8. Claim 4 objection due to informalities is maintained for the reasons set forth on page 4 of the previous Office Action.

Appropriate correction is required.

Status of Claim Rejections - 35 USC § 112

9. Claims 1-13 rejections under 35 U.S.C. 112, second paragraph are withdrawn.

Status of Claim Rejections - 35 USC § 102 and 103

10. Claims 1-9 and 11-13 rejections under 35 U.S.C. 103 are withdrawn.

11. Claims 1-9 and 11-13 rejections under 35 U.S.C. 102 are maintained for the reasons set forth on pages 6-8 of the previous Office action (see below).

Duncan, D. *et al.* teach a four component composition comprising: (i) a biologically active agent, *i.e.* immunogens or antigens at page 4, paragraph 1- page 5, paragraph 1, (ii) an adjuvant chemical having adjuvant properties, *i.e.* Pluronic® block copolymers, polycations, such as DEAE-4 dextran and polyarnithine at page 9, paragraph 1- page 10, paragraph 1, and (iii) an acceptable carrier, *i.e.* mucoadhesive at page 6, paragraph 1. Also pertaining to the applicant's instant claim 1 (iii), Duncan, J.D., *et al.* further teach the immunogen, mucoadhesive and adjuvant combined with a pharmaceutically acceptable liquid vehicle, *i.e.* water or buffered saline at page 11, paragraph 1. Duncan, J.D., *et al.* also teaches that an enhancement in immune response is observed when the adjuvant is combined with the immunogen and mucoadhesive, (iv) *i.e.* delivery system or vaccine for oral administration, at page 10, paragraph 2 - page 11, paragraph 3. Duncan, J.D., *et al.* also teach antigens incorporated into or attached to polymeric microparticles, nanoparticles, or liposomes are frequently more immunogenic at page 2.

The products of the prior art references of Duncan, J.D., *et al.* are in an analogous field of endeavor and appear to be the same as the pharmaceutical composition claimed by the applicant because they appear to possess the same or similar functional characteristics, i.e. microsphere prepared using a high molecular weight polymer of 100Kda or more and a composition wherein the ratio of the chemical (ii), *i.e.* Pluronic® block copolymers, polycations, such as DEAE-4 dextran and polyarnithine to the carrier is from 99.1 to 9.1 w/w (instant Claims 8, 9, and 11). The production of a composition by a particular process does not impart novelty to a composition when the same composition is taught by the prior art. This is particularly true when the properties of the composition are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Applicant urges that Claim Amendments:

1) exclude polyarnithine from the amended claims and in no way anticipates the present claims.

2) clarify the vitamin is water soluble and therefore does not encompass vitamin A,

3) further define the composition as a positively charged cationic block copolymer or positively charged cationic surfactant and that Duncan *et al.* reference do not include positively charged cationic block copolymers or surfactants in light of amended claims, and further the Pluronic ® trademark owner, BASF are non-ionic in nature as shown in the attached information from the BASF website and extracts from the Condensed Chemical Dictionary and Surfactant Systems, and further that the teachings of Duncan *et al.* in no way render the presently claimed invention anticipated since neither of these are block copolymers nor surfactants and do not fall within the terms of Claim 1(ii) (C) and that it could not be predicted with any reasonable degree of certainty that DEAE-4 dextran and polyarnithine would have adjuvant properties based upon the teachings of the Duncan reference.

Applicants arguments filed in the Office March 22, 2004 have been fully considered but they are not found persuasive. The Examiner respectfully acknowledges Pluronic ® trademark owner, BASF are non-ionic in nature, and although the Examiner appreciates the additional literature extracts, Applicants have not shown with certainty why the agent with an adjuvant is not taught by the general teachings of Duncan, *et al.* Neither polyarthinine nor polyornithine are elected species and although the Examiner mentions this by example, Applicants elected 1(ii)(C) now amended to read on a positively charged cationic block copolymer or a positively charged cationic surfactant that appear to be the same as taught by Duncan *et al.* (*i.e.* polycations, "...and other agents that can influence the structural or functional integrity of the mucosal surface to which they are applied" at page 10, 1st paragraph). Applicants have shown no side-by-side comparison between Duncan's and Applicants adjuvant and further in view of Applicants submission in the specification that "Particular cationic pluronics in category (C) above, are block copolymers or surfactants which are positively charged, in particular with $NH^{+}2$ groups [inherently a threonine analog of muramyl dipeptide contain $NH^{+}2$ in the amino acid side group

that is also an adjuvant in Duncan, *et al.* at page 9, paragraph 2]. These are available commercially for example for ICI Ltd (UK) sold under the trade names P101 and P121. **These may be used alone, but more preferably be used in combination with other adjuvants.** (emphasis added)", still anticipates the claimed invention.

New Grounds of Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

12. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of the claim is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation of "wherein the said" because it is unclear from the specification what applicant intends. Claim 1 from which it depends recites a 1st adjuvant. Clarification is required in order to overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 1-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Griffin, K.F. *et al.* 1998. (Vaccine 16(5): 517-521).

The Claims are drawn to a pharmaceutical composition comprising a biologically active agent, adjuvant chemical of positively charged cationic block copolymer or positively charged cationic surfactant, and carrier or diluent that generates a protective immune response and more specifically comprises a second adjuvant. Further claims are drawn to a microsphere, more specifically poly-(L-lactide), or liposome carrier, for mucosal surface or parenteral administration.

Griffin, K.F. *et al.* teach microencapsulation of V antigen (inherently a biologically active agent) with poly(L)lactide (inherently a 1st adjuvant)with a molecular weight of 2000 at page 517-518 (Materials and Methods). Griffin, K.F. *et al.* further teach microsphere compositions for double emulsion particles containing an aqueous solution of the V antigen of *Yersinia pestis*, or V antigen and IFN-γ (a cytokine recognized to have adjuvant properties, inherently a 2nd adjuvant) mixture with a 5% w/v solution of the polymer in co-encapsulated preparations wherein release studies were carried out in 20mM phosphate buffer (inherently a pharmaceutically acceptable carrier or diluent) at page 518, paragraphs 1-3 (see Table 1). Griffin, K.F. *et al.* also teach antibody responses for microsphere compositions administered by intraperitoneal inoculation to animals at page 519-520 (also see Material and Methods and Figures 1-2). Further the examiner is viewing the limitations such as in Claim 11, wherein the

composition of the poly(L)lactide to carrier is from 99:1 to 9:1 w/w is viewed as a limitation of optimizing experimental parameters.

Thus, Griffin, K.F. *et al.* anticipates the invention as claimed.

14. Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Park, J. *et al.* (US Patent 6,267,987 B1 published 31 Jul. 2001 with an earlier filing date of 11 Dec. 1998).

The Claims are drawn to a pharmaceutical composition comprising a biologically active agent, adjuvant chemical of positively charged cationic block copolymer or positively charged cationic surfactant, and carrier or diluent that generates a protective immune response and more specifically comprises a second adjuvant. Further claims are drawn to a microsphere, more specifically poly-(L-lactide), or liposome carrier, for mucosal surface or parenteral administration.

Park, J. *et al.* teach a positively-charged aminoalkyl polymers for use in the delivery of bioactive agents such as oligonucleotides (see abstract and column 3, lines 40 - 51). Park, J. *et al.* further teach components of the composition comprise an amphiphilic polyester block copolymer of poly(L-lactide), inherently a 1st adjuvant chemical coupled with poly[α-(ω-aminoalkyl) glycolic acid], inherently 2nd adjuvant chemical (also inherently a positively charged cationic block copolymer that is also a carrier of bioactive agents) at column 3, line 65 - column 4, line 17 (see claim 23). Park, J. *et al.* also teach bioactive agents and the biodegradable polyesters of the present invention are highly positively charged thereby greatly enhancing cellular and tissue uptake upon administration/delivery of bioactive agents at column 5, line 18 - column 6, line 52. Park, J. *et al.* further teach preferably diblock copolymers dispersions, *i.e.* microspheres of varying controlled particle size in water (inherently a pharmaceutically acceptable carrier or diluent) at column 7, line 51- column 8, line 34.

The Examiner further notes the products of the prior art references of Park, J. *et al.* are in an analogous field of endeavor and appear to be the same as the pharmaceutical composition

claimed by the applicant because they appear to possess the same or similar functional characteristics, *i.e.* microsphere of comprising high molecular weight coblock polymers of 100Kda or more and a composition wherein the ratio of the chemical (ii), *i.e.* poly(L-lactide) to the carrier is from 99.1 to 9.1 w/w at column 10, lines 38-53 (instant Claims 8-11). The production of a composition by a particular process does not impart novelty to a composition when the same composition is taught by the prior art. This is particularly true when the properties of the composition are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Thus, Park, J. *et al.* anticipates the invention as claimed.

15. Since the office does not have the facilities for examining and comparing applicants' pharmaceutical composition with the compositions disclosed in the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed pharmaceutical composition and the pharmaceutical composition of the prior art (*i.e.* that the pharmaceutical composition of the prior art does not possess the same material structural and functional characteristics of the claimed pharmaceutical composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald *et al.*, 205 USPQ 594.

Status of the Claims

16. No claims allowed.

Conclusion

17. The prior art of record and not relied upon is considered pertinent to applicant's disclosure.

a. Kotze, A.F. *et al.* 1997. N-trimethyl chitosan chloride as a potential absorption enhancer across mucosal surfaces: *in vitro* evaluation in intestinal epithelial cells (Caco-2). Pharmaceutical Research 14(9): 1197-1202.

b. Eyles, J.E. *et al.* 1998. Intra nasal administration of poly-lactic acid microsphere co-encapsulated Yersinia pestis subunits confers protection from pneumonic plague in the mouse. Vaccine: 16(7): 698-707.

18. Applicant's amendment necessitated the new grounds of rejection presented in theis Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (703) 305-4447. The examiner can normally be reached on Monday-Friday from 7am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the

organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Tammy K. Field
June 24, 2004

LYNETTE H. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600